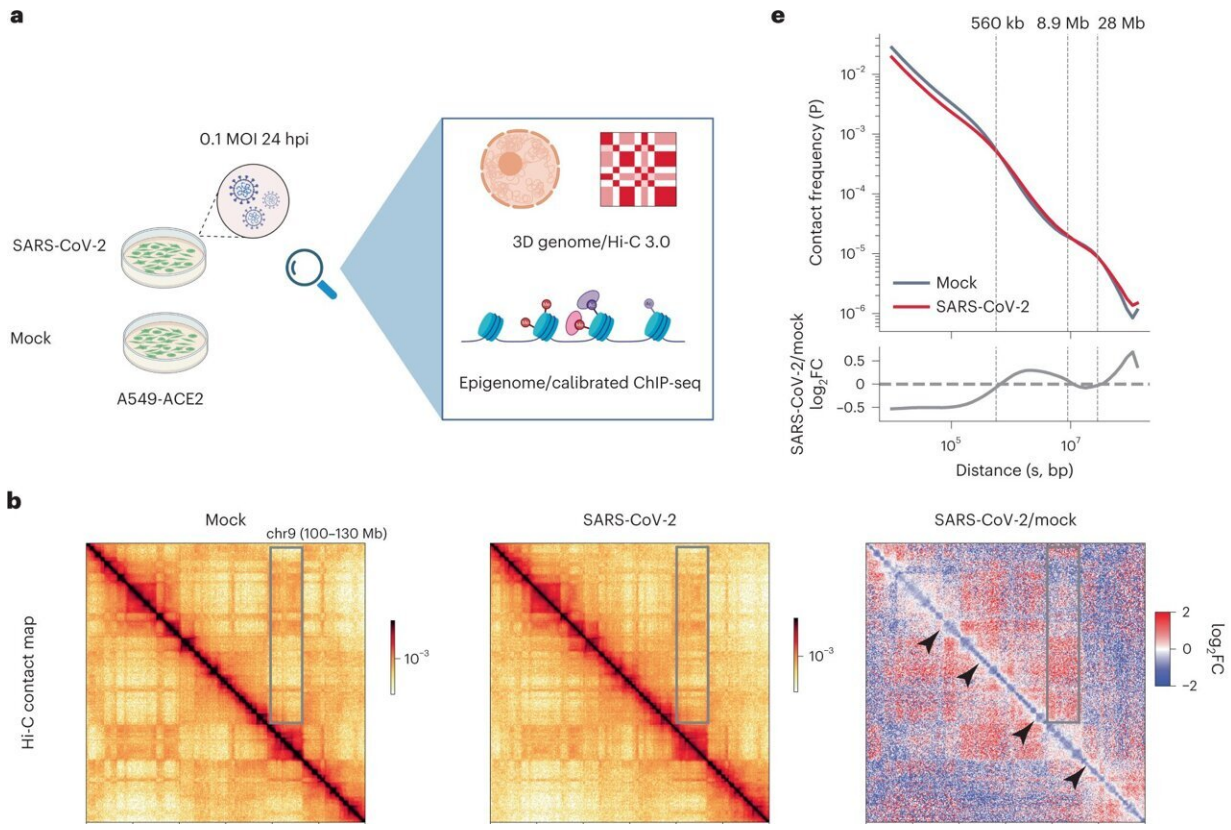
Study: SARS-CoV-2 can alter genome structure of our cells

March 23 2023



SARS-CoV-2 restructures the host 3D genome. a, The experimental design of this work. Created with BioRender.com. b, Hi-C 3.0 contact matrices of an example region (chr9: 100–130 Mb, hg19) in mock or infected conditions. Black arrowheads denote reduced short-distance interactions along the diagonal. Gray boxes show regions with altered compartmentalization. Bin size, 80 kb. c, Pearson correlation matrices of Hi-C 3.0 in the same region as in b. Arrowheads point to regions with virus-altered A–B (black) or A–A (cyan) compartmental interactions. Bin size, 80 kb. Color scales indicate Pearson correlation

coefficient (left and middle), and changes in the correlation matrices after infection (SARS-CoV-2/Mock, Pearson) are shown on the right. d, Zoom-in Hi-C snapshots of a 700 kb region in b and c (chr9: 95.7–96.4 Mb, hg19). Pink and cyan arrowheads show changed dot-shaped loops and domains, respectively. Bin size, 5 kb. e, Top: P(s) curve showing the relationship between the Hi-C contract frequency (P) of intra-chromosomal interactions ranked by genomic distance (s) in both mock (gray) and SARS-CoV-2 (red) conditions. Bottom: $\log_2$FC of Hi-C contact frequency ranked by distances (infection/mock), with dotted lines marking the crossing points of the two curves. In b and d, color scales indicate Hi-C contact frequencies (left and middle), and log2FC of SARS-CoV-2/mock contact frequencies (right). Credit: *Nature Microbiology* (2023). DOI: 10.1038/s41564-023-01344-8

People infected with SARS-CoV-2, the virus that causes COVID-19, may experience genome structure changes that not only may explain our immunological symptoms after infection, but also potentially link to long COVID, according to a new study by researchers at UTHealth Houston.

The study was published today in *Nature Microbiology*.

"This particular finding is quite unique and has not been seen in other coronaviruses before," said Wenbo Li, Ph.D., senior author on the study and associate professor in the Department of Biochemistry and Molecular Biology with McGovern Medical School at UTHealth Houston. "What we found here is a unique mechanism of SARS-CoV-2 that is associated with its severe impacts on human health."

The genetic materials in our cells are stored in a structure called chromatin. Some viruses of other categories have been reported to hijack or change our chromatin so that they can successfully reproduce in our cells. Whether and how SARS-CoV-2 may affect our chromatin was not known. In this study, researchers used leading-edge methods and

comprehensively characterized the chromatin architecture in human cells after a COVID-19 infection.

"We found that many well-formed chromatin architectures of a normal cell become de-organized after infection. For example, there is one type of chromatin architecture termed A/B compartments that can be analogous to the yin and yang portions of our chromatin. After SARS-CoV-2 infection, we found that the yin and yang portions of the chromatin lose their normal shapes and start to mix together. Such mixing may be a reason for some key genes to change in infected cells, including a crucial inflammation gene, interleukin-6, that can cause cytokine storm in severe COVID-19 patients," Li said.

In addition, this work found that chemical modifications on chromatin were also altered by SARS-CoV-2. "The changes of chemical modifications of chromatin were known to exert long-term effects on gene expression and phenotypes. Therefore, our finding may provide an unrealized new perspective to understand the viral impacts on host chromatin that can associate with long COVID," added Xiaoyi Yuan, who contributed to the research.

Nearly 1 in 5 Americans infected with COVID-19 are still suffering from long COVID symptoms even months after recovery from acute infection, according to the Centers for Disease Control and Prevention. Researchers hope these findings will pave the way into more research to understand the long-term impacts of the virus.

"Groundbreaking research frequently requires that scientists from different backgrounds, with different expertise, and from different departments come together and join in answering cutting-edge research questions," said Holger Eltzschig, MD, Ph.D., John P. and Kathrine G. McGovern Distinguished University Chair of the Department of Anesthesiology, Critical Care and Pain Medicine at McGovern Medical

School. "The highly collaborative research environment at UTHealth Houston fosters these opportunities. The Center for Perioperative Medicine at McGovern Medical School at UTHealth Houston provided the platform for our experts in SARS-CoV-2 infections, lung injury, epigenetics, and biochemistry to pursue this transformative research work together."

"This study elucidated to us how SARS-CoV-2 can uniquely alter our chromatin to cause COVID-19 symptoms. Future work will focus on understanding the mechanisms of how SARS-CoV-2 can achieve this. This will need to be done in both cell and animal models, and by using COVID-19 patients' samples. Finding the mechanism will offer therapeutic strategies to safeguard our chromatin and to better fight this virus," said Li.

More information: Ruoyu Wang et al, SARS-CoV-2 restructures host chromatin architecture, *Nature Microbiology* (2023). DOI: 10.1038/s41564-023-01344-8

Provided by University of Texas Health Science Center at Houston